Intention to Treat: Obstetrical Management at the Threshold of Viability

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Use of obstetrical interventions in the periviable period is more likely when parents desire active resuscitation and increases odds of survival to discharge from the NICU.

Short title:
Obstetrical Management at the Threshold of Viability

AJOG at a Glance:

A. This study was conducted to review the use of obstetrical interventions in multiple academic centers in the U.S. in deliveries prior to 25 weeks gestation, and to assess the odds of survival based on their usage.
B. Interventions were more likely to be used when resuscitation was desired. Increased survival was noted when pharmacologic interventions were bundled for deliveries occurring at 23 and 24 weeks gestation.
C. This study provides data on use of obstetrical interventions for management of pregnancies with threatened delivery prior to 25 weeks, including 22 week management, when interventions are more controversial.

ABSTRACT

Key words: Extremely preterm infants, obstetric interventions at viability, periviability

Background: Despite medical advances in the care of extremely preterm neonates, and growing acceptance of resuscitation at 23 and even 22 weeks' gestation, controversy remains concerning use of antepartum obstetrical interventions intended to improve outcomes in the setting of anticipated extremely preterm birth. In the absence of demonstrated benefit prior to 23 weeks, and with uncertain benefit at 23 weeks, prior obstetric committee opinions have advised against their use at these gestational ages.

Objectives:

- To review the use of obstetrical interventions at the threshold of viability based on neonatal resuscitation plan
- To review the odds of survival to NICU discharge based on use of obstetrical interventions while adjusting for neonatal factors

Study Design:
This retrospective study of 6 study centers reviewed pregnant patients admitted between 22 0/7 and 24 6/7 weeks facing delivery from 2011 to 2015. Patients with known anomalies or missing data were excluded. Records were reviewed for demographics, resuscitation plan, and obstetrical interventions. Mode of delivery, delivery room care, and final infant dispositions were recorded. Multiple gestations were included as one pregnancy in regard to the use of obstetrical interventions and were excluded from survival analysis.

Results:
478 mothers met inclusion criteria. When resuscitation was planned, mothers were more likely to receive all conventional obstetrical interventions (antenatal steroids, magnesium sulfate for neuroprotection, tocolytics, and *Group Beta Streptococcus* prophylaxis) regardless of gestational age at admission and were more likely to be delivered by cesarean section ($p<0.05$). Analyzed as a group, when antenatal steroids, magnesium sulfate, tocolytics and GBS prophylaxis were administered, the odds of survival to NICU discharge increased for newborns born at 22 weeks (OR 11.33, CI 1.405-91.4) and 23 weeks gestation (OR 15.5, CI 3.747-64.11) ($p<0.05$). In singletons, the odds of survival to NICU discharge was not improved by cesarean delivery versus vaginal delivery even after adjusting for use of additional interventions, weight, gender and gestational age (OR1.0, CI 0.59-1.8, $p=0.912$).

Conclusion:
In this study, when postnatal resuscitation was planned at 22 and 23 weeks gestation, women were more likely to receive antenatal steroids, magnesium sulfate, and antibiotics; provision of this bundle imparted survival benefit at 23 weeks but could not be demonstrated at 22 weeks due to small sample size. These findings support of

neonate-oriented obstetric interventions in the setting of delivery at 23 weeks when resuscitation is planned, and further exploration of optimal obstetric care when resuscitation of infants born at 22 weeks is anticipated.

Introduction

Periviable deliveries, occurring between approximately 20 0/7 weeks to 25 6/7 weeks, account for less than 1% of all births, but in some studies, up to 40% of all infant deaths [1-3]. While higher rates of neonatal active treatment have been shown to increase survival at the lowest gestational ages, obstetric interventions for these extremely premature infants have shown negligible improvement in survival rates and neurodevelopmental impairment [4] and clear guidelines for management are lacking [2, 4, 5]. Even without clear guidelines, some centers continue to push the boundaries for interventions in these extremely premature infants.

Common obstetrical interventions used for both prolongation of pregnancy and improvement of neonatal outcomes include antenatal steroids, tocolytics, magnesium sulfate for neuroprotection, antibiotics for *Group Beta Streptococcus* (GBS) prophylaxis, and cesarean delivery [6]. While the benefits of antenatal steroids have been documented, substantial uncertainty surrounds the benefit of the remainder of interventions for improving outcomes for extremely preterm infants, creating a potential disconnect between evidence-based obstetric recommendations and neonatal practice [1-4]. Some new studies also suggest benefits of antenatal steroids alone at these extremely early gestational ages with benefits seen following a full course of steroids as early as 22 weeks [7]. Therefore, the goal of this study was to evaluate the use of these interventions for pregnancies with threatened delivery between 22 0/7 to 24 6/7 weeks gestational age based on plans for resuscitation following delivery, and to determine the impact of these interventions on infant survival. Although these

interventions are not recommended, they are nonetheless utilized. We sought to understand the utilization of pharmacologic interventions for women based on their gestational-week of admission and neonatal consequences related to utilizing these interventions. We propose that while these interventions are not recommended at earlier gestational ages, they are nonetheless utilized, especially when resuscitation is planned for these early neonates.

Materials and Methods

We conducted a multi-center retrospective study consisting of INDEED (Investigating Neonatal Decisions for Extremely Early Deliveries) study group centers with data collected from January 1, 2011 to December 31, 2015. The primary aim of the INDEED study group was to understand conditions around decisions for active delivery room treatment for those pregnancies deliveries between 22 0/7 to 24 6/7 weeks gestational age. All participating hospitals were part of tertiary academic medical referral centers providing tertiary high-risk obstetric and neonatal care to high-risk obstetric patients. The Institutional Review Board reviewed and approved waiver of consent for this study at each individual site. A grant from North Shore University Health System supported use of the REDCap database [8].

Study Population

Both obstetrical and neonatal databases were reviewed for patients presenting between 22 0/7 to 24 6/7 weeks gestational age with a living fetus with threatened preterm delivery and delivering before 25 weeks; those who remained pregnant beyond

this periviable period were excluded. Women were excluded from the study if their fetus had a known major congenital or genetic anomaly. Women were analyzed by interventions received, regardless of singleton or multiple gestation to gauge rates of interventions or condition at delivery.

Study Institutions

Study institutions were located across the central regions of the United States. Resuscitation plans based on individual centers have previously been published by Dalia et al noting varying levels of resuscitation for all gestational age groups except those at 24 weeks. At 25 weeks gestational age, all interventions were provided for infants including resuscitation. During this review period, at two centers, options offered for newborn care at 22 completed weeks reportedly varied by neonatologists. Three had agreed-upon approaches by neonatology, and one had a written policy; of these centers, two offered only comfort care and two recommended comfort care but would provide resuscitation per parent request. Obstetric care for planned neonatal resuscitation was not standardized. The six centers were analyzed as having higher and lower resuscitation rates, based on significantly different rates of resuscitation at 22 and 23 completed weeks [9].

Data Collection

Records were reviewed for maternal demographic and medical information, plan of care for resuscitation through neonatal and/or obstetrical documentation and use of obstetric interventions and neonatal characteristics. Interventions reviewed include:

antenatal steroids (at least one dose prior to delivery), magnesium sulfate for neuroprotection, tocolytics (indomethacin, nifedipine, terbutaline or magnesium for tocolysis), antibiotics for GBS prophylaxis, and mode of delivery. For cesarean section, documented indications included fetal distress, fetal malpresentation, maternal well-being, a combination of the above, or unknown. Primary outcome of death vs. survival to NICU discharge of newborn was reported per each pregnancy.

Delivery room care was reviewed from both obstetrical and neonatal documentation. Gender, gestational age at delivery, and delivery weight (in grams) were collected as covariates. Documentation of delivery room resuscitation plan, (initiation of comfort care or neonatal resuscitation) was reviewed. Neonatal condition at delivery and death or survival to NICU discharge home were noted. Infants transferred to another center were not counted as having confirmed survival to NICU discharge, as their ultimate disposition was unknown.

Statistical Analysis

Descriptive statistics were calculated for the overall population and also for each gestational week at 22, 23 and 24 weeks. Summary statistics describing maternal characteristics compared to interventions used, stratified by the completed weeks gestation on presentation. Groups were analyzed using independent t-tests for continuous variables and chi-squared tests for categorical variables. Generalized linear models were created to note differences between intervention and non-intervention groups for antenatal steroids, magnesium sulfate, and GBS prophylaxis. Generalized linear mixed models were generated for differences between intervention and control

groups and included a random effect for the institution to account for the effect of different sites involved in the study.

Effects of obstetric interventions on survival to NICU discharge adjusted for neonatal characteristics were analyzed in step-wise manner. All newborns delivered between 22 and 24 completed weeks gestation for whom resuscitation was planned were analyzed first as one group, then by each gestational week. Multivariable logistic regression analyses evaluated effects of pharmacologic obstetric interventions, adjusting for neonatal characteristics, on survival to NICU discharge. Specifically, in our overall survival model for all 412 newborns with planned resuscitation, the effects on survival to discharge of the following variables were examined: receipt of any antenatal steroids, magnesium for neuroprotection, tocolytics, antibiotics for GBS prophylaxis and delivery by cesarean section, adjusting for neonatal factors known to influence survival: singleton status, sex, gestational age at delivery, and birthweight in grams. We subsequently modeled the effect of each pharmacologic intervention on survival to NICU discharge, controlling for neonatal factors. Post-hoc analyses to further examine findings at 24 weeks are explained in that section. Statistical analyses were performed using *SAS,* version 9.4 (SAS Institute, Cary, NC) and SigmaStat 4.0 (Systat Software Inc., San Jose, CA). P-values <0.05 were considered significant.

Results

478 pregnant women met inclusion criteria after 8 were excluded for fetuses with anomalies and 10 were excluded for missing medical records despite identification

in a database. Approximately one-third of these patients were nulliparous, with an average maternal age of 27.3 years. Gestational age at mother's admission ranged from 22 0/7 to 24 6/7 weeks, with mean and standard deviation 23 3/7 + 6 days. Gestational age at delivery (of twin A if multiple gestation) also ranged from). There were 398 singleton pregnancies with the remaining 80 comprised of twins (n=74 mothers) and higher order multiples (n=8 mothers).

Frequency of Obstetric Interventions by gestational age at admission

Baseline characteristics of women and receipt of obstetrical interventions are shown in Table 1. To understand the progression of care for women admitted at these early ages, we report here interventions received based on the gestational age at which women were first admitted. (In contrast, information on prevalence of interventions based on week of delivery are found in Table 2.) For the cohort, and for every gestational age group by week a plan for resuscitation was the most consistent factor associated with increased likelihood for receiving obstetric interventions. Maternal age, parity, and marital status did not appear to impact provision of these interventions. Estimated fetal weight was unknown prior to delivery for 27% (129 of 478) of women. A higher mean birthweight was also noted for those infants whose mothers received antenatal steroids, magnesium sulfate, and tocolytics.

<u>Women admitted at 22 weeks gestation</u>

143 pregnant women were admitted between 22 0/6 and 22 6/7; 33% (n=47) received at least one dose of steroids, 27% (n=38) received magnesium sulfate, 24% (n=34) received antibiotics for GBS prophylaxis, and 18% (n=26) received tocolytics prior

to delivery. Among those admitted at 22wks, 48% had a plan for resuscitation, and infants were delivered at 22 weeks (n=95), 23 weeks (n=33), and 24 weeks (n=15). Women planning neonatal resuscitation were more likely to receive steroids ($p<0.05$), magnesium sulfate ($p<0.05$), and GBS prophylaxis ($p<0.05$), but not tocolytics compared to those women not planning on neonatal resuscitation. Most (90%) of 22 week deliveries occurred vaginally. Cesarean section was performed in 20% (14 of 69) of cases in which neonatal resuscitation was planned and never when no resuscitation was planned (Table 1). The majority of these cases (12 of 14) were in the case of multiple gestations with the indication for singleton deliveries including malpresentation and maternal well-being.

Women admitted at 23 weeks gestation

197 pregnant women were admitted between 23 0/7 and 23 6/7; 72% (n=142) received at least one dose of steroids, 60% (n=118) received magnesium sulfate, 42% (n=84) received antibiotics for GBS prophylaxis, and 34% (n=68) received tocolytics prior to delivery, with planned resuscitation for 82% of infants. Among those admitted at 23 weeks, 117 delivered at 23 weeks and 80 delivered at 24 weeks. Women planning neonatal resuscitation were significantly more likely to receive all four interventions. Sixty-one percent of these pregnancies were delivered vaginally (n=117) with an increase in cesarean sections when neonatal resuscitation was planned (n=75 planned resuscitation, n=3 no resuscitation planned). Singleton deliveries accounted for 35% of cesarean deliveries with the most common indication being malpresentation (10 of 26).

Women admitted at 24 weeks gestation

138 women were admitted between 24 0/7 and 24 6/7; 81% (n=112) received at least one dose of steroids, 77% (n=106) received magnesium sulfate, 44% (n=61) received antibiotics for GBS prophylaxis, and 33% (n=46) received tocolytics prior to delivery, with planned resuscitation for 96% of infants. All patients planning resuscitation received steroids. Thirty-eight percent of pregnancies presenting at 24 weeks were delivered vaginally (n=42). Singleton deliveries accounted for 75% of cesarean deliveries with the most common indication being malpresentation (43 of 120). All patients included delivered prior to 25 weeks gestational age.

Impact of pharmacologic obstetrical interventions on confirmed survival to NICU discharge

Neonatal resuscitation was planned for 304 of the 397 mothers' newborns: 48%, 82%, and 96% at 22 weeks, 23 weeks, and 24 weeks gestational age, respectively. Receipt of maternal obstetric interventions and neonatal characteristics and outcomes for the 412 newborns with planned resuscitation are found in Table 2. Four-hundred twelve newborns had resuscitation planned; all but 13 (3%) were liveborn and admitted to the NICU. Because the ultimate dispositions for 13 NICU patients transferred outside facilities were not known, the confirmed survival to discharge home from the NICU for the entire group of newborns with resuscitation planned was admitted to the NICU was 45% (187 of 412).

For the entire group of 412 newborns with planned resuscitation, in the model analyzing survival as a function of maternal receipt of the 5 obstetric interventions (steroids, magnesium, tocolytics, GBS prophylaxis, cesarean delivery) and four neonatal

factors (gestational age, birthweight by week-specific study population quartiles, sex, and singleton status), three variables—steroids, gestational age, and birthweight—were significant. Amongst newborns with planned resuscitation, odds of confirmed survival to NICU discharge were 2.6 times higher for those whose mothers received antenatal steroids (CI: 1.3-5.6, p=0.011), after adjusting for the two other factors significant in the model—gestational age and birthweight.

In models analyzing the effect each medicinal intervention had on odds of survival while adjusting for the neonatal variables (age, sex, singleton, birthweight), again, only steroids were found to be significantly associated with survival to discharge (OR 2.7, CI: 1.5-4.9, p=0.002).

Newborns delivered 22 0/7 to 22 6/7 weeks

At 22 weeks, 36 of 40 newborns with planned resuscitation were liveborn, and condition of one was not known; 3 newborns were confirmed as surviving to discharge home. The outcomes in relation to exposures to maternal receipt of perinatal medications are reported in Figure 1. At 22 weeks, interventions did not result in significant differences in survival to home discharge, but sample size was small.

Newborns delivered 23 0/7 to 23 6/7 weeks

One-hundred twenty-two newborns delivered at 23 weeks had resuscitation planned; 116 (95%) were liveborn; 42 (34%) survived to discharge home from NICU, and one baby was transferred to an outside facility. As shown in Figure 1, for these newborns, the following interventions were associated with increased odds of confirmed survival to home from the NICU: antenatal steroids (OR 5.2, CI 1.8-14.6, p=0.002), magnesium (OR

4.3, CI 1.8-10.1, p=0.001, and bundle of receiving steroids, magnesium, GBS prophylaxis and tocolytics (OR 3.2, CI 1.2-8.7, p=0.037).

Newborns delivered 24 0/7 to 24 6/7 weeks

Two-hundred fifty newborns delivered at 24 weeks had resuscitation planned; 247 of these (99%) were liveborn. Fifty-seven percent (142 newborns of 250) survived to discharge home from NICU, and 11 were transferred to an outside facility. As seen in Figure 1, maternal receipt of obstetric interventions did not affect likelihood of survival to discharge home. Because these findings differed dramatically from those found for newborns delivered at 23 weeks, post hoc analyses were performed. The sample size of 250 newborns allowed performance of multivariable analyses of calculating odds of survival with each intervention while adjusting for neonatal factors of gestational age, birthweight and, sex, and singleton status. Birthweight was the only significant factor in these analyses. More specifically, birthweight lower than the lowest week-specific study group quartile was associated with lower odds of survival. However, as seen in Figure 2, the 24-week study population birthweight quartiles were markedly higher than even age-specific Fenton percentiles (average of male and female) [10], while those of the 23-week study population were closer to the Fenton percentiles. This may partially explain the dominance of birthweight on odds of survival to NICU discharge at 24 weeks while pharmacologic interventions were significantly associated with higher survival odds at 23 weeks.

Comment

Principal findings of this study

In this study, we sought to review the utilization of pharmacologic obstetric interventions and short-term neonatal survival across six academic centers. We found that when resuscitation was planned, mothers were more likely to receive all pharmacological interventions regardless of gestational age at admission. They were also more likely to be delivered by cesarean section.

Our findings suggest that, at these centers, obstetric practice is aligned with published obstetric practice guidelines at 24 weeks gestational age, but not at 22 and 23 weeks [2]. While there is no clear evidence in current literature to support antenatal steroids, magnesium sulfate, antibiotics, and cesarean delivery at 22 and 23 weeks, we found some of these patients did receive these interventions, particularly antenatal steroids; not surprisingly, provision of some of these interventions - antenatal steroids, magnesium sulfate, antibiotics for GBS, and cesarean delivery - was associated with a plan for neonatal resuscitation.

Newborns with planned resuscitation whose mothers received antenatal steroids had increased chances of survival to discharge home from the NICU in logistic regression models for the group as a whole and at 23 weeks. Unfortunately, our small sample size of 40 newborns delivered at 22 weeks precluded examining this group separately. We did not identify survival benefit associated with provision of pharmacologic interventions at 24 weeks; we speculate that the unusual weight distribution in this group of neonates may have overshadowed the influence of these interventions on survival to NICU discharge.

Results

Overall, our study findings are consistent with previous work demonstrating benefit of admission of antenatal steroids at earlier gestational ages. Mori et al. of Japan noted improved survival when antenatal steroids were used at 22 and 23 weeks [11]. Similar findings were noted by Hayes et al in the US when antenatal steroids were given at 23 weeks gestational age [12]. Study designs, however, have been small and retrospective and questions of equipoise may limit randomized controlled trials, leaving obstetricians with a lack of high-quality evidence or consensus on management. There has also been controversy around the best mode of delivery for these extremely premature infants, largely over concerns for increased maternal morbidities. Previous studies have shown little benefit to cesarean delivery over vaginal delivery prior to 24 weeks gestational age, though many physicians continue to offer cesarean delivery prior to this point [6, 13-16] . In our population, while cesarean delivery occurred in about half of deliveries overall, this had no significant effect on survival outcomes in the model examining all possible obstetric interventions and neonatal factors for newborns with planned resuscitation; closer examination of the impact of cesarean delivery is warranted as the aims of this study did not delve into the indications for cesarean deliveries.

Clinical Implications

As the care of extremely premature neonates becomes more advanced, we anticipated that while not recommended, use of these obstetrical interventions during this early gestational ages would continue based on the parents desire for neonatal

resuscitation. We recognize that while these results may not coincide with the most recent joint committee recommendations, these results may be used for future guidelines and discussion between both obstetricians and neonatologists for management.

While our findings demonstrate rates of interventions correlating to planned neonatal resuscitation at 22 weeks, our small cohort did not reveal statistically significant improvement in survival to NICU discharge. Our review of recent studies reporting survival rate at this gestational week (See Supplemental Table 1) reveals vast differences in reported survival rates. However, ours is the only study to our knowledge that reviews receipt of multiple interventions prior to delivery and impact on neonatal survival. We believe this adds to the discussion among obstetricians and neonatologists to review best practices among these extremely premature infants.

Research Implications

As we continue to review both this data and current literature, there are several questions regarding best practice management for these periviable deliveries. In the obstetric world, the role of cesarean section at these early gestational ages remains controversial prior to 24 weeks gestational ages. While full review of indications of delivery and outcome associations was beyond the scope of this analysis, it continues to warrant further research. We have also noticed differences among resuscitation

counseling and recognize this as an important area for further study.

Strengths and Limitations

While periviable deliveries make up a low percentage of preterm births, this study was able to include a large subset of deliveries across multiple perinatal centers. This robust group of data adds to current knowledge on management of these births and addresses both aspects of obstetric and neonatology management during the antepartum period. We recognize limitations of our study. Data were collected retrospectively from all study centers; prospective study might minimize missing data and more clarity about perinatal decision-making and neonatal outcome. Finally, new data and recommendations on management released by prominent pediatric and obstetric organizations during this time period may have led to changes in physician practices since the years of our study [2, 6].

Conclusions

Despite its limitations, this study contributes findings from nearly 500 women delivering in the periviable period to continue the discussion among obstetric and neonatal providers for best practices for treating mothers presenting in these extremely early gestational ages. While we do not offer a consensus for management at 22 and 23 weeks gestational age, the disconnect between existing guidelines and obstetric practice in this large cohort emphasizes the complexity of perinatal medical decision making for women at risk for extremely preterm delivery, particularly those desiring resuscitation for their infants after birth. If neonatal resuscitation is offered and planned, it is logical to offer interventions with potential to improve neonatal outcomes;

our findings suggest a discomfort among obstetric providers to forego potentially beneficial interventions, even in the absence of strong evidence to support their use. The demonstration of survival benefit for infants at 23 weeks when their mothers received these interventions supports continued close examination of existing guidelines; small numbers of infants born and resuscitated at 22 weeks continues to complicate evidence-based perinatal decision making when deliver at this gestational age is anticipated.

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References

1. BM, M., *Periviable birth and the shifting limit of viability.* Clinical Perinatology, 2017. **44**(2): p. 283-286.
2. Raju, T.N., et al., *Periviable birth: executive summary of a Joint Workshop by the Eunice Kennedy Shriver National Institute of Child Health and Human Development, Society for Maternal-Fetal Medicine, American Academy of Pediatrics, and American College of Obstetricians and Gynecologists.* J Perinatol, 2014. **34**(5): p. 333-42.
3. Marrs, C.C., et al., *Infant Outcomes after Periviable Birth: External Validation of the Neonatal Research Network Estimator with the BEAM Trial.* Am J Perinatol, 2016. **33**(6): p. 569-76.
4. Patel, R.M., et al., *Survival of Infants Born at Periviable Gestational Ages.* Clin Perinatol, 2017. **44**(2): p. 287-303.
5. Tucker Edmonds, B., et al., *Comparing obstetricians' and neonatologists' approaches to periviable counseling.* J Perinatol, 2015. **35**(5): p. 344-8.
6. American College of, O., Gynecologists, and M. Society for Maternal-Fetal, *Obstetric Care consensus No. 6: Periviable Birth.* Obstet Gynecol, 2017. **130**(4): p. e187-e199.
7. Travers, C.P., et al., *Mortality and pulmonary outcomes of extremely preterm infants exposed to antenatal corticosteroids.* Am J Obstet Gynecol, 2018. **218**(1): p. 130 e1-130 e13.
8. Harris, P.A., et al., *Research electronic data capture (REDCap)--a metadata-driven methodology and workflow process for providing translational research informatics support.* J Biomed Inform, 2009. **42**(2): p. 377-81.
9. Feltman, D.M., et al., *Antenatal Periviability Counseling and Decision Making: A Retrospective Examination by the Investigating Neonatal Decisions for Extremely Early Deliveries Study Group.* Am J Perinatol, 2019.
10. Tyson, J.E., et al., *Intensive care for extreme prematurity--moving beyond gestational age.* N Engl J Med, 2008. **358**(16): p. 1672-81.
11. Mori, R., et al., *Antenatal corticosteroids promote survival of extremely preterm infants born at 22 to 23 weeks of gestation.* J Pediatr, 2011. **159**(1): p. 110-114 e1.
12. Hayes, E.J., et al., *Effect of antenatal corticosteroids on survival for neonates born at 23 weeks of gestation.* Obstet Gynecol, 2008. **111**(4): p. 921-6.
13. Deutsch, A., et al., *Cesarean delivery versus vaginal delivery: impact on survival and morbidity for the breech fetus at the threshold of viability.* J Matern Fetal Neonatal Med, 2011. **24**(5): p. 713-7.
14. Deutsch, A.B., et al., *Cesarean or vaginal delivery for the breech fetus at the threshold of viability: results from a maternal-fetal medicine specialists survey.* J Matern Fetal Neonatal Med, 2011. **24**(3): p. 475-9.
15. Tucker Edmonds, B., et al., *Predictors of cesarean delivery for periviable neonates.* Obstet Gynecol, 2011. **118**(1): p. 49-56.

16. Tucker Edmonds, B., et al., *Morbidity and mortality associated with mode of delivery for breech periviable deliveries.* Am J Obstet Gynecol, 2015. **213**(1): p. 70 e1-12.

Tables and Figures:

Table I: Characteristics and Receipt of Obstetric Interventions of 478 pregnant women
*Significant at <0.05 level
**Significant at <0.01 level

Table 2: Newborns with planned resuscitation: Clinical characteristics, perinatal interventions and outcomes by delivery week
*Reflects use estimated fetal weight within one week of birth when birthweight unknown, n=7; missing weights (birth or delivery-week estimated fetal weight data), n=17
**Unknown condition at birth, but did not survive to NICU admission

Figure 1: Use of interventions and survival based on gestational age at delivery
*p<0.05

Figure 2: Distribution of birthweights of 412 newborns with planned resuscitation
*F refers to Fenton curve percentiles (mean of female/male)

Supplemental Table 1: Studies since 2015 including 22 week liveborn newborns, perinatal management, and survival

Table I: Characteristics and Receipt of Obstetric Interventions of 478 pregnant women overall and by gestational age in weeks

	Overall (N = 478)																							
	Antenatal Steroids			Magnesium sulfate			Tocolytics			GBS PPX			Mode of Delivery											
	Yes	No		Yes	No		Yes	No		Yes	No		Vaginal	Cesarean										
Mother's age	27.7 (6.4)	27.0 (6.0)		27.0 (6.1)	27.6 (6.3)		26.6 (6.2)	27.5 (6.1)		27.3 (6.2)	27.2 (6.2)		27.2 (6.0)	27.4 (6.5)										
Birthweight	419.0 (240.8)	290.5 (196.1)	**	412.8 (242.0)	330.7 (216.5)	**	459.9 (231.3)	342.2 (228.5)	**	381.8 (247.5)	382.4 (228.1)		365.5 (226.9)	410.5 (247.3)										
Parity																								
Nulliparous	(51.33%)	89 (50.28%)		139 (53.05%)	104 (48.37%)		78 (55.71%)	165 (48.96%)		92 (51.69%)	151 (50.50%)		157 (52.51%)	86 (48.31%)										
Multiparous	146 (48.67%)	88 (49.72%)		123 (46.95%)	111 (51.63%)		62 (44.29%)	172 (51.04%)		86 (48.31%)	148 (49.50%)		142 (47.49%)	92 (51.69%)										
Race/Ethnicity									*															
Caucasian	104 (34.67%)	46 (26.44%)		87 (33.46%)	63 (29.44%)		52 (37.41%)	98 (29.25%)		53 (29.78%)	97 (32.77%)		92 (30.98%)	58 (32.77%)										
African American	171 (57%)	107 (61.49%)		151 (58.08%)	127 (59.35%)		81 (58.27%)	197 (58.81%)		108 (60.67%)	170 (57.43%)		176 (59.26%)	102 (57.63%)										
Other	25 (8.33%)	21 (12.07%)		22 (8.46%)	24 (11.21%)		6 (4.32%)	40 (11.94%)		17 (9.55%)	29 (9.80%)		29 (9.76%)	17 (9.6%)										
Marital Status																								
Single	204 (67.77%)	121 (68.36%)		176 (67.18%)	149 (68.98%)		91 (65%)	234 (69.23%)		116 (64.8%)	209 (69.90%)		209 (69.67%)	116 (65.17%)										
Married	97 (32.23%)	56 (31.64%)		86 (32.82%)	67 (31.02%)		49 (35%)	104 (30.77%)		63 (35.2%)	90 (30.10%)		91 (30.33%)	62 (34.83%)										
Insurance			*						*															
Medicaid	178 (59.53%)	106 (60.92%)		151 (58.08%)	133 (62.44%)		75 (53.96%)	209 (62.57%)		101 (57.06%)	183 (61.82%)		173 (58.45%)	112 (63.28%)										
Private	106 (35.45%)	49 (28.16%)		95 (36.54%)	60 (28.17%)		58 (41.73%)	97 (29.04%)		65 (36.72%)	90 (30.41%)		96 (32.43%)	58 (32.77%)										
None	15 (5.02%)	19 (10.92%)		14(5.38%)	20 (9.39%)		6 (4.32%)	28 (8.38%)		11 (6.21%)	23 (7.77%)		27 (9.12%)	7 (3.95%)										
Desired resuscitation?			**			**			*			**			**									
Yes	281 (93.67%)	84 (48.55%)		244 (93.13%)	121 (57.35%)		123 (87.86%)	242 (72.67%)		166 (93.26%)	199 (67.46%)		190 (64.63%)	174 (97.75%)										
No	19 (6.33%)	89 (51.45%)		18 (6.9%)	90 (42.65%)		17 (12.14%)	91 (27.33%)		12 (6.74%)	96 (32.54%)		104 (35.37%)	4 (2.25%)										

	22 Weeks (N = 143)																							
	Antenatal Steroids			Magnesium sulfate			Tocolytics			GBS PPX			Mode of delivery											
	Yes	No		Yes	No		Yes	No		Yes	No		Vaginal	Cesarean										
Mother's age	28.9 (5.3)	27.2 (6.1)		27.8 (5.4)	27.7 (6.1)		29.3 (6.4)	27.4 (5.6)		29.4 (5.7)	27.2 (5.9)		27.6 (6.0)	29.3 (4.8)										
Birthweight	349.7 (214.1)	256.8 (198.9)	*	348.5 (217.7)	267.1 (200.4)		388.3 (209.6)	270.1 (203.3)	*	257.7 (208.3)	317.9 (209.5)		295.9 (207.5)	320.1 (241.1)										
Parity																								
Nulliparous	24 (52.17%)	55 (57.29%)		23 (60.53%)	56 (53.85%)		13 (50%)	66 (56.9%)		14 (42.42%)	65 (59.63%)		71 (55.47%)	8 (57.14%)										
Multiparous	22 (47.83%)	41 (42.71%)		15 (39.47%)	48 (46.15%)		13 (50%)	50 (43.10%)		19 (57.58%)	44 (40.37%)		57 (44.53%)	6 (42.86%)										
Race/Ethnicity									*						*									
Caucasian	19 (40.43%)	22 (23.16%)		16 (42.11%)	25 (24.04%)		13 (50%)	28 (24.14%)		13 (38.24%)	28 (25.93%)		34 (26.56%)	7 (50%)										
African American	23 (48.94%)	63 (66.32%)		18 (47.37%)	68 (65.38%)		12 (46.15%)	74 (63.79%)		18 (52.94%)	68 (62.96%)		82 (64.06%)	4 (28.57%)										
Other	5 (10.64%)	10 (10.53%)		4 (10.53%)	11 (10.58%)		1 (3.85%)	14 (12.07%)		3 (8.82%)	12 (11.11%)		12 (9.38%)	3 (21.43%)										
Marital Status			*						*			*			*									
Single	24 (51.06%)	69 (71.88%)		21 (55.26%)	72 (68.57%)		12 (46.15%)	81 (69.23%)		16 (47.06%)	77 (70.64%)		88 (68.22%)	5 (35.71%)										
Married	23 (48.94%)	27 (28.13%)		17 (44.74%)	33 (31.43%)		14 (53.85%)	36 (30.77%)		18 (52.94%)	32 (29.36%)		41 (31.78%)	9 (64.29%)										

Insurance					*		**					
Medicaid	22 (46.81%)	56 (60.22%)		17 (44.74%)	61 (59.8%)	6 (23.08%)	72 (63.16%)	15 (45.45%)	63 (58.88%)		71 (56.35%)	7 (50%)
Private	20 (42.55%)	24 (25.81%)		18 (47.37%)	26 (25.49%)	18 (69.23%)	26 (22.81%)	14 (42.42%)	30 (28.04%)		37 (29.37%)	7 (50%)
None	5 (10.64%)	13 (13.98%)		3 (7.89%)	15 (14.71%)	2 (7.69%)	16 (14.04%)	4 (12.12%)	14 (13.08%)		18 (14.29%)	0
Desire for resuscitation?			**		**					**		**
Yes	38 (82.61%)	31 (33.33%)		31 (81.58%)	38 (37.62%)	16 (61.54%)	53 (46.9%)	24 (72.73%)	45 (42.45%)		55 (44%)	14 (100%)
No	8 (17.39%)	62 (66.67%)		7 (18.42%)	63 (62.38%)	10 (38.46%)	60 (53.10%)	9 (27.27%)	61 (57.55%)		70 (56%)	0

23 Weeks (N = 197)

	Antenatal Steroids			**Magnesium sulfate**		**Tocolytics**			**GBS PPX**		**Mode of delivery**	
	Yes	**No**		**Yes**	**No**	**Yes**	**No**		**Yes**	**No**	**Vaginal**	**Cesarean**
Mother's age	26.9 (6.3)	27.8 (6.7)		26.7 (6.3)	27.7 (6.5)	25.6 (6.1)	27.9 (6.4)		27.0 (6.6)	27.2 (6.2)	27.2 (6.2)	26.9 (6.7%)
Birthweight	411.9 (244.3)	339.3 (179.8)	*	409.6 (246.4)	367.5 (203.4)	462.4 (233.9)	348.1(220.2)	**	391.7 (242.2)	396.4 (225.5)	399.5 (220.6)	391.5 (248.8%)
Parity												
Nulliparous	76 (53.52%)	23 (41.82%)		65 (55.08%)	34 (43.04%)	40 (58.82%)	59 (45.74%)		47 (55.95%)	52 (46.02%)	57 (48.31%)	42 (53.85%)
Multiparous	66 (46.48%)	32 (58.18%)		53 (44.92%)	45 (56.96%)	28 (41.18%)	70 (54.26%)		37 (44.05%)	61 (53.98%)	61 (51.69%)	36 (46.15%)
Race/Ethnicity												
Caucasian	48 (33.8%)	19 (35.9%)		37 (31.62%)	30 (38.46%)	23 (34.33%)	44 (34.38%)		24 (28.57%)	43 (38.74%)	43 (36.75%)	23 (29.87%)
African American	84 (59.15%)	28 (52.83%)		72 (61.54%)	40 (51.28%)	41 (61.19%)	71 (55.47%)		55 (65.48%)	57 (51.35%)	62 (52.99%)	50 (64.94%)
Other	10 (7.04%)	6 (11.32%)		8 (6.84%)	8 (10.26%)	3 (4.48%)	13 (10.16%)		5 (5.95%)	11 (9.91%)	12 (10.26%)	4 (5.19%)
Marital Status												
Single	102 (71.83%)	35 (63.6%)		85 (72.03%)	52 (65.82%)	46 (67.65%)	91 (70.54%)		60 (71.43%)	77 (68.14%)	82(69.49%)	55 (70.51%)
Married	40 (28.17%)	20 (36.4%)		33 (27.97%)	27 (34.18%)	22 (32.35%)	38 (29.46%)		24 (28.57%)	36 (31.86%)	36 (30.51%)	23 (29.49%)
Insurance												
Medicaid	92 (65.25%)	33 (60.00%)		78 (66.67%)	47 (59.49%)	45 (67.16%)	80 (62.02%)		54 (64.29%)	71 (63.39%)	71 (60.17%)	54 (70.13%)
Private	46 (32.62%)	17 (30.91%)		36 (30.77%)	27 (34.18%)	21 (31.34%)	42 (32.56%)		26 (30.95%)	37 (33.04%)	41 (34.75%)	21 (27.27%)
None	3 (2.13%)	5 (9.09%)		3 (2.56%)	5 (6.33%)	1 (1.49%)	7 (5.43%)		4 (4.76%)	4 (3.57%)	6 (5.08%)	2 (2.6%)
Desire for resuscitation?			**		**			*			**	**
Yes	131 (92.25%)	31 (57.41%)		110 (93.22%)	52 (66.67%)	62 (91.18%)	100 (78.13%)		82 (97.62%)	80 (71.43%)	86 (73.5%)	75 (96.15%)
No	11 (7.75%)	23 (42.59%)		8 (6.78%)	26 (33.33%)	6 (8.82%)	28 (21.88%)		2 (2.38%)	32 (28.57%)	31 (26.5%)	3 (3.85%)

24 Weeks (N = 138)

	Antenatal Steroids			**Magnesium sulfate**		**Tocolytics**		**GBS PPX**		**Mode of delivery**	
	Yes	**No**		**Yes**	**No**	**Yes**	**No**	**Yes**	**No**	**Vaginal**	**Cesarean**
Mother's age	26.3 (5.8)	29.8 (6.9)	*	27.0 (6.1)	26.8 (6.3)	26.6 (5.9)	27.2 (6.3)	26.6 (5.6)	27.3 (6.5)	26.1 (5.4)	27.5 (6.5)
Birthweight	460.4 (241.9)	285 (217.0)	*	444.0 (243.6)	422.8 (256.3)	502.3 (235.3)	409.4 (245.0)	448.2 (253.2)	433.7 (239.4)	436.9 (247.1)	442.4 (245.2)
Parity											
Nulliparous	54 (48.21%)	11 (42.31%)		51 (48.11%)	14 (43.75%)	25 (54.35%)	40 (43.48%)	31 (50.82%)	34 (44.16%)	29 (55.77%)	36 (41.86%)
Multiparous	58 (51.79%)	15 (57.69%)		55 (51.89%)	18 (56.25%)	21 (45.65%)	52 (56.52%)	30 (49.18%)	43 (55.84%)	23 (44.23%)	50 (58.14%)
Race/Ethnicity											
Caucasian	37 (33.33%)	5 (19.23%)		34 (32.38%)	8 (25.00%)	16 (34.78%)	26 (28.57%)	16 (26.67%)	26 (33.77%)	14 (27.45%)	28 (32.56%)
African American	64 (57.66%)	16 (61.54%)		61 (58.10%)	19 (59.38%)	28 (60.87%)	52 (57.14%)	35 (58.33%)	45 (58.44%)	32 (62.75%)	48 (55.81%)

Other	10 (9.01%)	5 (19.23%)		10 (9.52%)	5 (15.63%)		2 (4.35%)	13 (14.29%)	9 (15.00%)	6 (7.79%)	5 (9.80%)	10 (11.63%)
Marital Status												
Single	78 (69.64%)	17 (65.38%)		70 (66.04%)	25 (78.13%)		33 (71.74%)	62 (67.39%)	40 (65.57%)	55 (71.43%)	39 (75.00%)	56 (65.12%)
Married	34 (30.36%)	9 (34.62%)		36 (33.96%)	7 (21.88%)		13 (28.26%)	30 (32.61%)	21 (34.43%)	22 (28.57%)	13 (25.00%)	30 (34.88%)
Insurance						*						
Medicaid	64 (57.66%)	17 (65.38%)		56 (53.33%)	25 (78.13%)		24 (52.17%)	57 (62.64%)	32 (53.33%)	49 (63.64%)	30 (58.82%)	51 (59.30%)
Private	40 (36.04%)	8 (30.77%)		41 (39.05%)	7 (21.88%)		19 (41.30%)	29 (31.87%)	25 (41.67%)	23 (29.87%)	18 (35.23%)	30 (34.88%)
None	7 (6.31%)	1 (3.85%)		8 (7.62%)	0		3 (6.52%)	5 (5.49%)	3 (5.00%)	5 (6.49%)	3 (5.88%)	5 (5.81%)
Desire for resuscitation?			**									
Yes	112 (100%)	22 (84.62%)		103 (97.17%)	31 (96.88%)		45 (97.83%)	89 (96.74%)	60 (98.36%)	74 (96.10%)	49 (94.23%)	85 (98.84%)
No	0	4 (15.38%)		3 (2.83%)	1 (3.13%)		1 (2.17%)	3 (3.26%)	1 (1.64%	3 (3.90%)	3 (5.77%)	1 (1.16%)

*Significant at <0.05 level.

**Significant at <0.01 level.

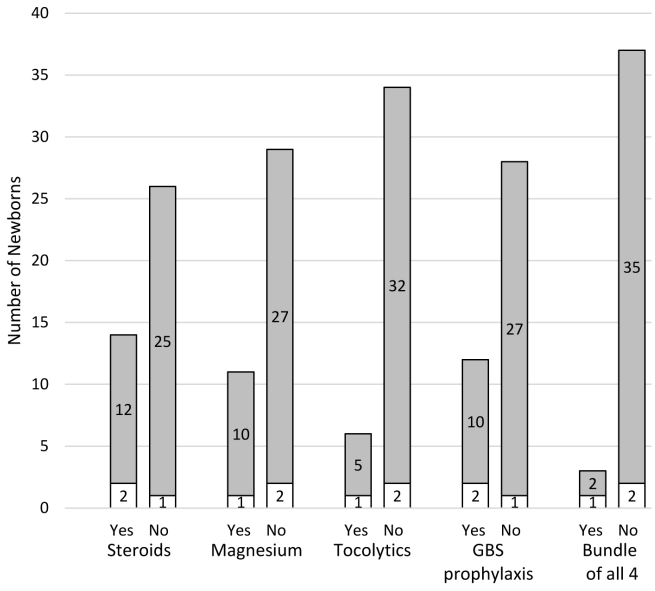
Table 2: 412 newborns with planned resuscitation: clinical characteristics, perinatal interventions and outcomes by delivery week

	22 0/7 - 22 6/7 n=40	23 0/7 - 23 6/7 n=122	24 0/7 - 24 6/7 n=250	**All gestational ages n=412**
Perinatal interventions n (%) or mean±SD (range)				
Antenatal steroids (partial or complete course)	14 of 40 (35%)	84 of 122 (69%)	220 of 250 (88%)	318 of 412 (77%)
Gestational weeks at OB admission	22.4 ±0.3 (22.0-22.8)	23.2 ±0.3 (22.1-23.9)	23.9 ±0.6 (22.0-24.9)	23.6 ±0.7 (22.0-24.9)
Age at receipt, weeks	22.3 ±0.5 (21.0-22.9)	23.3 ±0.4 (21.7-23.9)	24.0 ±0.5 (22.6-24.9)	23.8 ±0.6 (21.0-24.9)
Hours between last steroid dose and delivery (of Baby A)	40.9 ±48 (1.4-164)	33.7 ±44(0.33-249)	73.1 ±71 (0-280)	61.3 ±66 (0-280)
Magnesium for neuroprotection	11 of 40 (28%)	70 of 122 (57%)	197 of 250 (79%)	278 of 412 (68%)
Tocolytics	6 of 40 (15%)	39 of 122 (32%)	98 of 246 (40%)	143 of 408 (35%)
Cesarean delivery	2 of 40 (5%)	38 of 120 (32%)	160 of 250 (64%)	200 of 410 (49%)
Neonatal characteristics				
Gestational weeks at OB admission	22.4 ±0.3 (22.0-22.8)	23.2 ±0.3 (22.1-23.9)	23.9 ±0.6 (22.0-24.9)	23.6 ±0.7 (22.0-24.9)
Gestational weeks at delivery	22.5 ±0.3 (22.0-22.9)	23.5 ±0.3 (23.0-23.9)	24.4 ±0.3 (24.0-24.9)	24.0 ±0.7 (22.0-24.9)
Birthweight, g mean±SD (range)* 25%ile, 75%ile	497 ±64 (295-502) 457, 547	574 ±95 (310-880) 505,640	660 ±115 (280-1060) 590, 730	619 ±119 (280-1060) 540, 691
Singleton delivery	26 of 40 (65%)	89 of 122 (73%)	193 of 250 (77%)	308 of 412 (75%)
Male sex	24 of 40 (60%)	65 of 122 (53%)	130 of 250 (52%)	219 of 412 (53%)
Neonatal outcomes				
Liveborn	36 of 39 (92%)**	116 of 122 (95%)	247 of 250 (99%)	399 of 411 (97%)
Survival to NICU discharge	3 of 39 (8%)	42 of 121 (35%)	142 of 239 (59%)	187 of 399 (47%)
Survival to NICU discharge or transfer to other facility	4 of 40 (10%)	43 of 122 (35%)	153 of 250 (61%)	200 of 412 (49%)
Liveborn baby surviving to discharge home from NICU	3 of 35 (9%)	42 of 115 (37%)	142 of 247 (58%)	187 of 399 (47%)
Liveborn baby discharged home or transferred from NICU	4 of 36 (11%)	43 of 116 (37%)	153 of 247 (62%)	200 of 399 (50%)

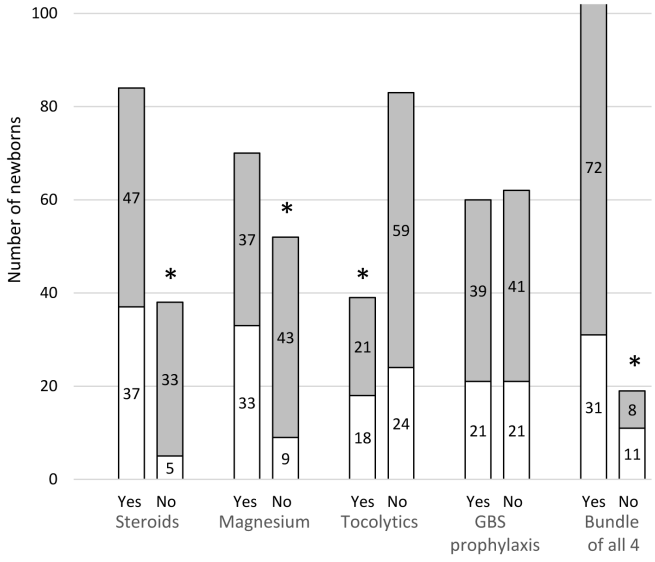
*Reflects use estimated fetal weight within one week of birth when birthweight unknown, n=7; missing weights (birth or delivery-week estimated fetal weight data), n=17

**Unknown condition at birth, but did not survive to NICU admission

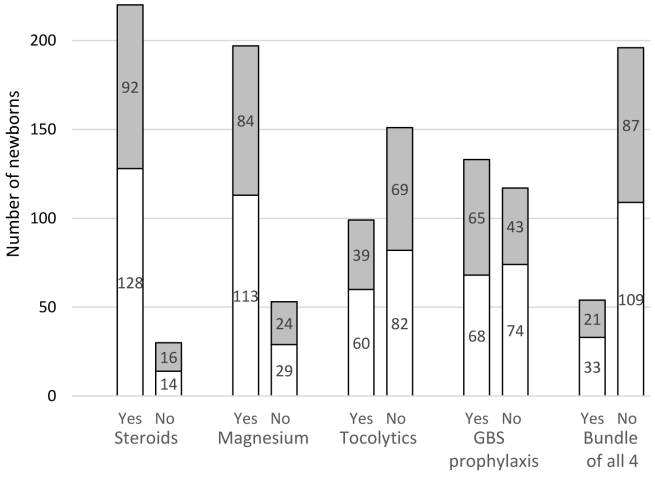
Newborns born at 22 weeks (n=40)

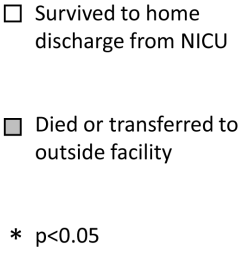


Newborns born at 23 weeks (n=122)



Newborns born at 24 weeks (n=150)





Distribution of birthweights of 412 newborns with planned resuscitation

T Caps 10th and 90th percentiles study newborns
Boxes 75th and 25th percentiles
-- -- -- --Mean
----------Median
+ 5th and 95th percentiles
*F Fenton curve percentiles (mean of female/male)